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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/852,261	05/10/2001	Geoffrey Goldspink	117-351	5457

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EXAMINER	
NICHOLS, CHRISTOPHER J	
ART UNIT	**PAPER NUMBER**
1647	13

DATE MAILED: 11/20/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/852,261	GOLDSPINK ET AL.	
	Examiner	Art Unit	
	Christopher Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8.October.2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *7,8,12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 9-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-13* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *14 December 2001* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/852,261* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7,9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I (Claims 1-6 and 9-11), drawn to a method of treating nerve damage comprising administering to a subject an effective amount of an MGF (mechano-growth factor) Insulin-like Growth Factor I (IGF-I) isoform comprising amino acid sequence encoded by nucleic acid sequence of IGF-I exons 4, 5, and 6 in Paper No. 12 (8 October 2002) is acknowledged. The traversal is on the ground(s) that Groups I, II, III, IV, V, and VI do not represent six patentably distinct inventions. The Applicant further notes that Groups II, III, IV, and V are all dependent on claim 1 therefore a search of Groups I, II, III, IV, and V would be co-extensive. Also, the separate Grouping of the subject matter of Groups II-IV (i.e. claims 7 and 8) may deny the Applicants the opportunity to amend their claims during prosecution to recite the subject matter of originally filed dependent claims. Finally, the Applicant notes that Group VI contains elements required to practice the method of the elected Group I such that a search of the elected Group would include a search of the kit of Group VI. Applicant's arguments have been fully considered but are not found to be persuasive. This is not found persuasive because, with regard to Groups I, II, III, IV, and V, each represents a separate and distinct invention, wherein search and consideration of each invention is not co-extensive between the individual groups. Group I requires search and consideration of treating nerve damage using MGF (mechano-growth factor) Insulin-like Growth Factor I (IGF-I) isoform comprising amino acid sequence encoded by nucleic acid sequence of IGF-I exons 4, 5, and 6, which is not required of the other Groups. Group II requires search and consideration of a method treating a muscle, which is not required of the other Groups. Group II requires search

and consideration of gene therapy, which is not required of the other Groups. Group IV requires search and consideration of using a polypeptide growth factor other than MGF, which is not required of the other Groups. Group V requires search and consideration of using "another neurologically active agent", which is not required of the other Groups. Therefore, an undue search burden is required of the examiner to search all of the peptides together. Also, Group VI requires "a further polypeptide growth factor which prevents or diminishes degeneration" and "another neurologically active agent" which are not essential elements of Group I. Therefore, Group VI represents a separate and distinct invention. Furthermore, Group I can be practiced without the kit of Group VI. The restriction requirement is maintained. Claims 7-8 and 12-13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected material, there being no allowable generic or linking claim. Claims 1-6 and 9-11 will be examined to the extent that they read on to a method of treating nerve damage comprising administering to a subject an effective amount of an MGF (mechano-growth factor) Insulin-like Growth Factor I (IGF-I) isoform comprising amino acid sequence encoded by nucleic acid sequence of IGF-I exons 4, 5, and 6.

Status of Application, Amendments, and/or Claims

2. The preliminary amendments of 14 December 2001 and 27 August 2002 (Paper No.'s 8 and 11) has been entered in full. The sequence listing has been found to be free of errors and has been entered into the file. Claims 7-8 and 12-13 are withdrawn from consideration, as discussed above. Claims 1-6 and 9-11 are under examination.

3. To aid in correlating any papers for this application, all correspondence regarding this application should be directed to Art Unit 1647, Examiner Christopher Nichols.

Priority

4. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in parent Application No. 09/852261, filed on 10 May 2001.

Specification

5. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

6. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (pp. 19 line 11). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-6 and 9-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. Claims 1 is directed to a method of treating nerve damage comprising administering SEQ ID NO's: 2, 4, or 6. Claim 2 is directed to the method of claim 1 wherein the nerve damage is to a peripheral nerve. Claim 3 is directed to the method of claim 1 wherein said MGF peptides are localized to the site of nerve damage by means of a conduit. Claim 4 is directed to the method of claim 1 wherein the conduit comprises poly-3-hydroxy-butyrate (PHB). Claim 5 is directed to the method of claim 1 wherein the nerve damage comprises the severing of the nerve. Claim 6 is directed to the method of claim 2 wherein said treatment of said nerve damage is combined with a treatment that prevents or diminishes degeneration of the target organ that the damaged nerve innervates. Claim 9 is directed to the method of claim 1 wherein said MGF has the ability to reduce motorneuron loss by 50% or greater or 80% or greater in response to nerve avulsion. Claim 10 is directed to the method of claim 1 wherein said MGF is unglycosylated. Claim 11 is directed to the method of claim 1 wherein said MGF is SEQ ID NO's: 2, 4, or 6.

8. The specification teaches that MGF is expressed in skeletal and cardiac muscle tissue in response to stretch and exercise and as a result is believe to be involved in repair of damage to muscle. Chew et al. (1995) and Yang et al. (1996) use the name IGF-I Ec that is equivalent to MGF in the instant application. On the subject of conduits, poly-3-hydroxy-butyrate (PHB) conduits have been shown to assist in nerve regeneration and to show good results compared to nerve autografts.

9. The prior art teaches that motorneuron cell death occurs under pathological conditions including ischemia, traumatic injury, and neurodegenerative diseases. A dramatic loss of motoneurons is observed after axonal injury in neonatal rats and mice; both excitotoxicity and apoptotic cell death appear to be involved in the mechanisms leading to rapid loss of the injured motorneurons. Given the responsiveness of motorneurons to a variety of neurotrophic factors, the motorneurons appear to be dependent on multiple growth and trophic molecules for normal development and/or maintainace (Vejsada et al., 1998). MGF is an isoform of Insulin-like growth factor-I (IGF-I); a pleiotropic trophic factor with a wide spectrum of actions on different CNS and PNS tissues that belongs to a family of structurally related proteins (Dore et al., 1997). The biological actions of the IGFs are modulated by a family of at least six IGF-binding proteins that monitor the bioavailability of the IGFs and their interaction with the IGF receptors. IGF appears to be involved in multiple aspects of development and regeneration of the neuromuscular system. Expression levels of IGFs during muscle development correlate with the extent of neuromuscular synaptogenesis than with muscle growth or early differentiation. IGFs may be important components in promoting and accelerating peripheral nerve regeneration and functional recovery after lesions. It therefore appears that IGFs may play multiple and important

roles in neuromuscular development and regeneration (Caroni et al., 1994). However, mechano-growth factor (MGF) is only detected in overloaded or damaged skeletal muscle and is derived from the IGF-1 gene by alternative splicing under these conditions (McKoy et al., 1999). Thus it is not clear what role MGF plays in injury and recovery. Further, the many facets of peripheral nerve damage and recovery are not adequately outlined in the specification to support a commanding role by MGF in repair and regeneration of peripheral nerve damage.

10. The scope of patent protection sought by Applicant as defined by the claims fails to correlate reasonably with the scope of enabling disclosure provided by the specification and prior art for the following reasons.

11. Regarding nerve damage, the art recognizes the enormous range of injuries that constitute nerve damage including but not limited to severance, avulsion, compression, and bruising. Due to the large quantity of experimentation necessary to evaluate the effects of SEQ ID NO.'s 2, 4, and 6 on all types of nerve damage, the lack of direction/guidance presented in the specification regarding study of SEQ ID NO.'s 2, 4, and 6's effect on all nerve damage, the absence of working examples directed to administering SEQ ID NO.'s 2, 4, and 6 to damaged nerves, the complex nature of the invention, the unpredictability of effects any peptide would have on any damaged nerves (Vejsada et al., 1995; Vejsada et al., 1998; EPO 0 308 386 A1), and the breadth of the claims which fail to recite limitations which types of nerve damage, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

12. Regarding homologues, the art recognizes that even minor alterations to protein structure have unpredictable effects on a proteins function. Due to the large quantity of experimentation

necessary to identify all the applicable homologues of SEQ ID NO.'s 2, 4, and 6, the lack of direction/guidance presented in the specification regarding synthesizing, screening, and evaluating homologues of SEQ ID NO.'s 2, 4, and 6, the absence of working examples directed to homologues of SEQ ID NO.'s 2, 4, and 6, the complex nature of the invention, the unpredictability of the effects of mutation on protein structure and function (Ngo et al., 1994; Wells, 1990; Vejsada et al., 1995; Chew et al., 1995; Jansen et al. 1991; Vejsada et al., 1998), and the breadth of the claims which fail to recite limitations for what constitutes an homologue, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

13. Regarding preventing or diminishing degeneration, the art recognizes that target organs can be glands, muscles among other varieties of tissue. Due to the large quantity of experimentation necessary to identify all the applicable target organs, the lack of direction/guidance presented in the specification regarding evaluating the progression and cessation of degeneration in any given target organ, the absence of working examples directed to the effects of SEQ ID NO.'s 2, 4, and 6 on any given target organ, the complex nature of the invention, the unpredictability of the effects of peptides on any given organ or tissue (Vejsada et al., 1995; Lundborg et al., 1997; Vejsada et al., 1998; Goldspink, 1999; EPO 0 308 386 A1), and the breadth of the claims which fail to recite limitations for what constitutes preventing or diminishing degeneration of a given target organ, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

14. Thus the claimed invention is directed to a method of using MGF to treat peripheral nerve damage, including but not limited to severed peripheral nerves, which is contrary to the

teachings of the prior art. One skilled in this art would be expected to reasonably doubt that the claimed method would work due to the following obstacles: expectation of target organ recovery, does MGF peptide have any effect on nervous tissue?, and the expectation of nervous regeneration. The specification does not provide guidance on how to overcome expected obstacles. Due to the large quantity of experimentation required to determine how to administer MGF peptides to achieve rejoining of severed peripheral nerves, the specification's lack of guidance regarding how to overcome expected obstacles, the lack of working examples directed to administering the MGF peptides to injured nerves, the contrary state of the art, the unpredictability of what is needed to overcome the obstacles, and the large breadth of the claims, undue experimentation would be required of the skilled artisan to practice the claimed methods.

Summary

15. Claims 1-6 and 9-11 are hereby rejected.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher Nichols, PhD whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, PhD can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

CJN
November 19th, 2002

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher Nichols, PhD whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:30AM to 5:00PM.

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Elyabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

CJN
October 28th, 2002